Non-Scientific ABSTRACT

Patients bearing tumors of different histologic origin have elevated levels of Transforming Growth Factors-βs (TGF-βs). TGF-βs are growth factors that are associated with immunosuppression. Suppression of the patients' immune system results in their inability to recognize and destroy tumors when they first appear. Furthermore, suppression of patients' immunity makes them susceptible to frequent infections. We have shown that injection of genetically engineered tumor cells to block their TGF-β production makes the gene modified cells potent vaccines that are recognized by and can activate the immune system against the tumor. Activation of the immune system subsequently causes the recognition and control of the parental, unmodified tumors in the host organisms. We have shown this phenomenon to be true in animal tumor models and in human clinical trials. Thus, we propose to use this approach in a phase II clinical trial in patients with stages II, IIIA, IIIB and IV non-small cell lung cancers. The two and five year survivals for stage IIIB are 10.8 and 3.9 and for stage IV are 5.4 and 1.3 percent respectively. The five year survival for stages II-IV is 7.5%.

In this Phase II clinical trial we will use four human non-small cell lung cancer cell lines that have been previously established in tissue culture laboratory. We will gene modify these tumor cells in the laboratory to block their TGF-β secretion. We will inject the genetically engineered cells as vaccines in patients with stages II to IV non-small cell lung cancer. Patients will be injected four times, in monthly intervals, with the gene modified vaccine cocktails that consist of the four non-self (allogeneic) TGF-β antisense gene modified tumor cell. Our rationale for using other people's tumor cells is that lung tumor cell lines belonging to different people have been shown to share common characteristics that are recognized by non-self immune systems. Treated patients will be evaluated four months after they enter therapy. Patients that respond to therapy will receive an additional four to twelve injections to evaluate whether their response to therapy can be amplified.

Response, time to tumor progression, and tumor free survival will be monitored in patients and compared with historical controls and patients receiving other forms of therapy. Patients will be monitored and evaluated according to standard evaluation criteria of no response, stable disease, partial response and complete response. The results of this study will be used to evaluate the feasibility of a phase III clinical trial with TGF-β antisense gene modified tumor cells alone and in combination with IL-2 gene modification.